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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,604	02/19/2002	R. Tyler White	056324-0129	2755

22428 7590 04/21/2004

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,604	WHITE ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *80 and 81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *80 and 81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 80 and 81 are pending.

Election/Restrictions

Applicant's election with traverse of SEQ ID NO:208 in Paper filed April 2, 2004 is acknowledged. The traversal is on the ground(s) that "there is no undue burden to search all of the sequences" (Response, page 1). This is not found persuasive because the examination of methods of use of all polypeptides together requires not only the search of 40 sequences but an additional consideration of a method of use of each recited polypeptide. The polypeptides recited in claims 80 and 81 are structurally different polypeptides having different functions, i.e. inhibiting different serine proteases (see, for example, Figures 45 and 46 A-D). Therefore, methods of inventions I-XL produce different therapeutic effects and have different utilities.

The requirement is still deemed proper and is therefore made FINAL.

Claims 80 and 81 have only been examined with respect to the polypeptide of SEQ ID NO: 208 (BG022).

Claim Objections

Claims 80 and 81 are objected to as reciting non-elected polypeptides of SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:183, SEQ ID NO:185, SEQ ID NO:186, SEQ ID

NO:187, SEQ ID NO:188, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:194, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO: 204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:210, SEQ ID NO:212, SEQ ID NO: 213, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:223 and SEQ ID NO:224.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications.

Appropriate correction is required.

Information Disclosure Statement

The instant application contains no IDS.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. 37 CFR 1.821(d) requires the use of assigned sequence identifier

in all instances where the description or claims of a patent application discuss sequences. With regard to the drawings, the sequence identifier must be used either in the drawing or in the Brief Description of the Drawings. The following are examples of the incompliance with the Sequence Rules: Figures 2, 4, 5, 7, 8, etc.; pages 23, 35-38, 40-49, 51, 52, 54, 56.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 80 and 81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a clinical condition associated with increased activity of kallikrein, plasmin and Factor XIIa and a method of inhibiting activity of kallikrein, plasmin and Factor XIIa in a mammal using a polypeptide of SEQ ID NO:208, does not reasonably provide enablement for a method of treating a clinical condition associated with increased activity of any serine protease and a method of inhibiting activity of any serine protease in a mammal using a polypeptide of SEQ ID NO:208. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The serine proteases belong to a multigene family of enzymes having different structures, functions and producing different effects. As a result, inhibitors of one serine protease not necessarily have an effect on the other serine protease. The specification teaches that a Kunitz Protease Inhibitor (KPI) polypeptide of SEQ ID NO:208 (BG022) is a potent inhibitor of kallikrein, plasmin and Factor XIIa (Figure 46D). At the current state of the art, the correlation between the structure and function of a polypeptide remains highly unpredictable, and the specification teaches no other serine proteases that are inhibited by KPI of SEQ ID NO:208. The specification teaches that a KPI with a potency towards kallikrein, plasmin and Factor XIIa can be used in a clinical condition associated with blood loss such as during cardiopulmonary bypass (CPB) surgery (e.g., pages 1-6). However, a KPI of SEQ ID NO:208 cannot be used in treatment of clinical conditions associated with increased activities of any serine proteases. For example, having no known inhibitory potency towards chymotrypsin or trypsin, a KPI of SEQ ID NO:208 will not be useful in treatment of various gastrointestinal conditions associated with increased activities of chymotrypsin, trypsin, pepsin, etc. Therefore, based on the

unpredictable nature of the invention and the state of the prior art, the lack of guidance and working examples, and the extreme breadth of the claims, one skilled in the art could not use the polypeptide of SEQ ID NO:208 to treat clinical conditions associated with increased activity of serine proteases other than kallikrein, plasmin and Factor XIIa and could not use a polypeptide of SEQ ID NO:208 to inhibit serine proteases other than kallikrein, plasmin and Factor XIIa in a mammal without undue experimentation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

April 16, 2004